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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/890,371	04/08/2002	Gregor Cevc	266/034	1865

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EXAMINER	
HISSONG, BRUCE D	
ART UNIT	PAPER NUMBER
1646	

SHORTENED STATUTORY PERIOD OF RESPONSE	NOTIFICATION DATE	DELIVERY MODE
3 MONTHS	01/29/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Notice of this Office communication was sent electronically on the above-indicated "Notification Date" and has a shortened statutory period for reply of 3 MONTHS from 01/29/2007.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	09/890,371	CEVC ET AL.	
	Examiner	Art Unit	
	Bruce D. Hissong, Ph.D.	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 October 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *54-104* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *54-104* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/30/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Formal Matters

1. Applicants' reply to the office action mailed on 7/26/2006, including arguments/remarks and amendments to the claims, was received on 10/30/2006 and has been entered into the record.

2. Claims 54-104 are currently pending and are the subject of this office action.

3. The text of those sections of Title 35, U.S.C. not included in this action can be found cited in full, in the previous office action mailed on 7/26/2006.

Information Disclosure Statement

The information disclosure statement received on 10/30/2006 has been fully considered.

Specification

The objection to the specification regarding improper use of trademarks, as set forth on page 2 of the office action mailed on 7/26/2006, is *maintained*. In the response received on 10/30/2006, the Applicants argue that the trademarks were properly capitalized and accompanied by a statement of generic subject matter.

These arguments have been considered and are not persuasive. Although the specification adequately describes Tween 20 and Tween 80 in generic terms, the recitation of "a suspension of carriers loaded with insulin" (p. 41, last paragraph) does not adequately describe Transfusulin™ because there is no information whatsoever as to what the suspended carriers are. Similarly, the recitation of "a sorbitane monoalkylate" does not adequately describe Span™ or Arlacel™ in generic terms because the specification does not specifically that which sorbitane monoaklylate(s) make up Span™ or Arlacel™.

Claim Objections

1. Objection to claim 58, as set forth on page 3 of the office action mailed on 7/26/2006, is *withdrawn* in response to Applicants' amendments to the claim to recite "a compound that is a cytokine or a compound that induces.....".

2. Objection to claim 97 for failing to further limit the subject matter of claim 92, as set forth on page 3 of the office action mailed on 7/26/2006, is *withdrawn* in response to Applicants' amendment to claim 97 to recite "at least two doses of vaccine".

Claim Rejections - 35 USC § 112, first paragraph – enablement

Rejections withdrawn

1. Rejection of claim 64 under 35 USC § 112, first paragraph, regarding lack of enablement for a method for transporting an agent across any barrier except mucosal/nasal barriers, as set forth on pages 5-6 of the prior office action mailed on 7/26/2006, is *withdrawn* in response to Applicants' amendment to the claim to specifically recite transport across of mucosal barrier.

2. Rejection of claims 54-104 under 35 USC § 112, first paragraph, regarding lack of enablement for a compound comprising, or a method of transnasally administering a composition comprising any non-protein/peptide active agent, as set forth on pages 3-4 of the prior office action mailed on 7/26/2006, is *withdrawn* in response to Applicants' arguments that the specification provides numerous examples of allergens, antigens, and other active ingredients suitable for use in the instant invention. These active ingredients disclosed in the instant specification include proteins, peptides, nucleic acids, carbohydrates, polysaccharides, pathogens, and various types of drugs. Furthermore, the Applicants argue that the specification, on page 40, discloses methods for making highly adaptable penetrant carriers and that these methods are generic and without limitation in regards to the active ingredient. Thus, by following the instant specification, one of ordinary skill in the art would know how to make and use a composition that is commensurate in scope with the claims, wherein the active

ingredient of said composition is not limited to protein/peptide agents. These arguments have been fully considered and are persuasive.

Rejections maintained

3. Claims 54-104 *remain rejected* under 35 USC § 112, first paragraph, regarding lack of enablement for a compound comprising, or a method of transnasally administering a composition comprising a penetrant comprised of any two substances other than a surfactant and a lipid, as set forth on pages 4-5 of the prior office action mailed on 7/26/2006.

In the response received on 10/30/2006, the Applicants argue that the specification provides information on how to prepare penetrants, and recites examples of lipids and surfactants that can be used. Specifically, the specification provides examples for preparing a penetrant comprised of a phospholipid and a surfactant, and therefore one of ordinary skill in the art would know how to make and use the claimed penetrant.

These arguments have been fully considered and are not persuasive. Although the specification does teach various examples of lipids and surfactants that can be used in the claimed penetrant, including specific phospholipids and surfactants, the breadth of the claims as currently written encompass a penetrant comprised of any two substances that differ by at least a factor of 10 in solubility, and the ability to form homo/hetero-aggregates. Thus, the claims are drawn to a potentially large number of combinations of any two substances. The specification only provides examples showing a penetrant comprised of a phospholipid and a surfactant, and therefore one of ordinary skill in the art would not be able to predict which of the many possible combinations of two substances could also act as a penetrant for transnasal transport of all possible active ingredients. Therefore, one of ordinary skill in the art would require further, undue experimentation in order to make and use a penetrant comprised of any two substances other than a phospholipid and a surfactant.

Other issues

It is noted that no rejection under 35 U.S.C. 112, first paragraph, enablement, is being made over claim 100 in regards to the various diseases recited in the claim. Although Applicants are reciting a large number of diseases, the claimed invention is drawn to a method for administration, rather than a method of treating any specific disease. As such, any novelty of the claimed invention, if it was indeed novel, would be in regards to the claimed

penetrant/carrier, and not in regards to compounds for treatment of any specific disease, for which a sufficient number of compounds/compositions are known in the art.

Claim Rejections - 35 USC § 112, first paragraph – written description

Rejections withdrawn

1. Rejection of claims 93 and 102 under 35 USC § 112, first paragraph, regarding lack of written description for "fragments" or "derivatives" of a pathogen extract, or an antigen "derived" from a pathogen, as set forth on page 7 of the prior office action mailed on 7/26/2006, is withdrawn in response to Applicants' arguments that the specification provides examples of various pathogens and examples of pathogen-derived antigens (e.g. cholera toxin, heat labile toxin, tetanus toxin).

These arguments have been fully considered and are found persuasive.

Rejections maintained

2. Claim 60 *remains rejected* under 35 USC § 112, first paragraph, regarding lack of written description for any derivative or analog of an anti-cytokine antibody, as set forth on pages 6-7 of the prior office action mailed on 7/26/2006.

In the response received on 10/30/2006, the Applicants argue that the specification teaches various antibody fragments, including Fc, Fab, and F(ab')2 fragments, and therefore provides adequate written description for the claimed genus of antibody derivatives or analogs.

These arguments have been fully considered and are not found persuasive. Although the specification provides examples of well-known antibody fragments, the specification does not define or provide examples of any antibody "analog", or other "derivative" of an antibody, and therefore the specification does not adequately describe the claimed genus, which encompasses antibody fragments, and also any potential "analog" of an antibody or any potential molecule that is "derived" from an antibody.

Claim Rejections - 35 USC § 112, second paragraph

Rejections withdrawn

1. Rejection of claims 54-104 under 35 USC § 112, second paragraph, as being indefinite in regards to the phrase "and/or" as set forth on pages 7-8 of the prior office action mailed on 7/26/2006, is withdrawn in response to Applicants' arguments that the claims are not intended to recite Markush groups, and thus do not employ standard Markush format, and instead simply recite alternative characteristics of a composition, and thus the use of the phrase "and/or" is clear and definite.

2. Rejection of claim 61 under 35 USC § 112, second paragraph, as being indefinite regarding how a cytokine activity can be physically associated with the claimed penetrant, as set forth on page 8 of the prior office action mailed on 7/26/2006, is *withdrawn* in response to Applicants' amendments to the claim to recite a "compound that is a cytokine or induces cytokine or anti-cytokine activity".

3. Rejection of claim 83-86 under 35 USC § 112, second paragraph, as being indefinite regarding insufficient antecedent basis for the term "the relative drug or agent", as set forth on page 8 of the prior office action mailed on 7/26/2006, is *withdrawn* in response to Applicants' amendments to the claims to recite "the active ingredient".

Rejections maintained

4. Claim 81 *remains rejected* under 35 USC § 112, second paragraph, as being indefinite in regards to "practically sufficient", as set forth on page 9 of the prior office action mailed on 7/26/2006. In the response received on 10/30/2006, the Applicants deleted the term "practically sufficient penetrant stability" from the claim. However, the claim still recites a biocompatible solution that has "practically sufficient" transport rate across a barrier. As set forth in the previous office, action, the claim does define the metes and bounds of "practically sufficient", and therefore the claim is indefinite.

5. Claim 55 *remains rejected* under 35 USC § 112, second paragraph, as being indefinite in regards to "two forms" of a substance, as set forth on page 8 of the prior office action mailed on 7/26/2006.

In the response received on 10/30/2006, the Applicants argue that page 14 of the instant specification clearly defines "two forms" of a substance, and one of skill in the art would understand that "etc." merely refers to the inclusion of other such modifications that do not change a compound to another compound, and therefore the phrase "two forms" of a substance is clear and definite.

These arguments have been fully considered and are not found persuasive. As set forth in the previous office action, defining the term "two forms of a substance" as "two ionization states or salt forms of the same substance, two different complexes of the substance, etc." Because the inclusion of "etc" in the definition can encompass almost anything and is therefore open-ended, the term "two forms of a substance" is indefinite in light of the definition recited in the instant specification.

6. Claim 64 *remains rejected* under 35 USC § 112, second paragraph, as being indefinite in regards to the term "large common structures", as set forth on page 8 of the prior office action mailed on 7/26/2006.

In the response received on 10/30/2006, the Applicants amended the claim to recite a "mucosal barrier", and therefore the claim is no longer indefinite to the metes and bounds of the term "barrier". Regarding the phrase "large common structures", the Applicants argue that the term is clear and definite to one of ordinary skill in the art, and "large common structures" that may be formed by the penetrant components encompass more complex structures having, e.g. larger size and higher molecular weight. Furthermore, the Applicants argue that page 28 of the instant specification discloses that the "common large structures" are "typically in the form of a physical or chemical complex."

These arguments have been fully considered and are not found persuasive. Although the "large common structures" can be complex structures having larger size and higher molecular weight, the term is not necessarily limited to these structures. Furthermore, the specification does not describe or teach which types of physical or chemical complexes give rise to a "large common structure". Because the term "large common structure" is not limited to the definition provided by the Applicants, the metes and bounds of the term are not clear.

7. Claim 66 *remains rejected* under 35 USC § 112, second paragraph, as being indefinite in regards to "surfactant-like" molecules, as set forth on page 9 of the prior office action mailed on 7/26/2006.

In the response received on 10/30/2006, the Applicants argue that the term "surfactant-like" is well-known in the art, and is clearly described in the specification in the paragraph bridging pages 27-28.

These arguments have been fully considered and are not persuasive. The instant specification provides examples of various surfactants that can be used in the composition of the instant invention. However, the specification does not define the term "surfactant-like" in such a way as to distinguish "surfactant-like" molecules from actual surfactant molecules. The metes and bounds of the term are not clear because the claim is drawn to any molecule that is "like" a surfactant, in any way and by any degree.

Claim Rejections - 35 USC § 102

Claim 104 *remains rejected* under 35 USC § 102(b) as being anticipated by Cevc *et al* (*Biochem Biophys Acta*, 1998, Vol. 1368, No. 2, pages 201-215), as set forth on pages 9-10 of the office action mailed on 7/26/2006.

In the response received on 10/30/2006, the Applicants argue that amended claim 104 is now drawn to a composition comprising an active ingredient and a transnasal carrier, and that because Cevc *et al* does not specifically recite a "transnasal" carrier, and does not specifically recite the particular claimed characteristics, it does not meet the limitations of the claim as currently amended.

These arguments have been fully considered and are not found persuasive. As set forth in the previous office action mailed on 7/26/2006, Cevc *et al* teach a composition comprising an active ingredient, and further comprising two additional components. Specifically, the two additional components are phosphatidylcholine and sodium cholate, which are taught by the specification to be preferred components of the claimed penetrant. Although Cevc *et al* does not specifically disclose a "transnasal" carrier, it is noted that this is merely an intended use and is given no patentable weight in the instant case. Furthermore, it is also noted that the composition of Cevc *et al* contains the same active ingredients and other components as the examples of the instant specification, and in the absence of evidence to the contrary, would be

expected to possess the particular characteristics recited in the claims. Therefore, because Cevc *et al* teaches a composition identical to that of the claimed invention, the disclosure of Cevc *et al* meets the limitations of claim 104.

Claim Rejections - 35 USC § 103

Claims 54-103 *remain rejected* under 35 USC § 103(a) as being obvious in view of the combination of Cevc *et al*, Drejer *et al* (*Diabetic Med*, 1992, Vol. 9, pages 335-340), and Hussain *et al* (US 4,383,993) as set forth on pages 10-12 of the office action mailed on 7/26/2006.

In the response received on 10/30/2006, the Applicants argue that claims 54-103 are not obvious in view of this combination of references because the claimed combination of references does not teach or suggest a method of *transnasally* administering an active ingredient in a composition comprised of the claimed penetrant. The Applicants further argue that there is no motivation to combine the teachings of Drejer *et al* and Hussain *et al* because the two references do not suggest that combining Tween 80 and phosphatidylcholine would result in any useful composition for use in a method of transnasal administration. Furthermore, the Applicants argue that Cevc *et al* teaches away from the claimed invention, and thus a person of ordinary skill in the art would not expect that an active ingredient such as insulin could be transnasally administered using a composition comprising the claimed penetrant. Therefore there would be no motivation to combine Cevc *et al*, Drejer *et al*, and Hussain *et al*.

These arguments have been fully considered and are not persuasive. As discussed above and in the previous office action mailed on 7/26/2006, Cevc *et al* teaches a composition for administration of insulin, wherein said composition comprises insulin, phosphatidylcholine (a lipid), and sodium cholate (a surfactant). Drejer *et al* teaches transnasal administration of insulin using a composition comprising phosphatidylcholine, while Hussain *et al* teaches transnasal administration of progesterone using a composition comprising Tween 80. Therefore, the teachings of Drejer *et al* and Hussain *et al* would show a skilled artisan that both phosphatidylcholine and lipids such as Tween 80 are useful components of compositions for transnasal administration. Because Cevc *et al* teaches a composition comprising an active ingredient (insuline) and further comprising phosphatidylcholine and a lipid (sodium cholate), one of ordinary skill in the art would have the motivation to use the composition disclosed by

Cevc *et al* for transnasal administration of various active ingredients such as insulin or progesterone. Therefore, because both phosphatidylcholine and Tween 80 are disclosed as being useful for transnasal administration, one of ordinary skill in the art would also have a reasonable expectation of success of transnasally administering an active ingredient in a composition combining both phosphatidycholine and a lipid such as sodium cholate or Tween 80. Furthermore, although Cevc *et al*, Drejer *et al*, and Hussain *et al* do not specifically teach compositions for transnasal administration of active ingredients such as allergens, antigens, cytokines, or agents that induce anti-cytokine activity, it would be obvious to one of ordinary skill in the art to transnasally administer these types of compounds using the composition taught by Cevc et al because the polypeptide compounds insulin and progesterone can be transnasally administered, and thus a skilled artisan would expect that these polypeptide/peptide compounds could also be transnasally administered. Finally, while Cevc *et al*, Drejer *et al*, and Hussain *et al* do not specifically recite a composition with a specific diameter of the penetrant, or any specific concentration of the penetrant, one of ordinary skill in the art would have the motivation, and the ability, to optimize the composition of Cevc *et al* in order to achieve efficient transnasal transport of any active ingredient.

Conclusion

No claim is allowable.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bruce D. Hissong, Ph.D., whose telephone number is (571) 272-3324. The examiner can normally be reached M-F from 8:30 am - 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, Ph.D., can be reached at (571) 272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

BDH
Art Unit 1646

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